

CLAIMS

1. A genetic construct which comprises a nucleotide sequence of interest (NOI) and splice-functional element(s) selected and arranged such that the first open reading frame (ORF) available for translation in a target cell population is for the NOI while in non-target cells the NOI ORF is absent or is not the primary ORF.
2. A construct as claimed in claim 1 wherein the protein expression product of the NOI is generated by a *cis*-splicing mechanism.
3. A construct as claimed in claim 1 or claim 2 wherein the NOI is a therapeutic gene.
4. A construct as claimed in claim 3 wherein the NOI encodes a cytotoxic agent.
5. A construct as claimed in any preceding claim wherein the target cell population is a malignant cell population.
6. A construct as claimed in any preceding claim wherein the NOI is not expressed as a fusion product with one or more exons or partial exons from within the splice-functional elements.
7. A construct as claimed in any preceding claim wherein said splice-functional elements include the B-tropomyosin exon 5 splice donor and/or the B-tropomyosin exon 7 splice acceptor.
8. A construct as claimed in any one of claims 1 to 6 wherein said splice-functional elements include human FGFR α -exon.

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9. A construct as claimed in claim 8 wherein the target cell population comprises glioblastoma related/derived cells.
- 5 10. A construct as claimed in any one of claims 1 to 6 wherein the splice-functional elements include the mitochondrial ATP synthase γ subunit.
- 10 11. A construct as claimed in any one of claims 1 to 6 wherein the splice-functional elements include regions from within the human non-muscle myosin heavy chain B.
12. An mRNA molecule derived from a genetic construct as defined in any preceding claim.
- 15 13. A protein molecule obtained by expression of a genetic construct as defined in any one of claims 1 to 11.
- 20 14. A vector incorporating a genetic construct as claimed in any one of claims 1 to 11.
- 25 15. A cell comprising a construct, nucleic acid or protein molecule or vector as claimed in any preceding claim.
16. A construct or vector as claimed in any one of claims 1 to 11 or 14 for use in therapy.
- 30 17. Use of a construct or vector as claimed in any one of claims 1 to 11 or 14 in the manufacture of a medicament whose physiological effect is restricted to a target cell population and which treats a disease characterised in that it is responsive to expression of
- 35 an exogenously administered gene.

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18. A pharmaceutical formulation comprising a construct or vector as claimed in any one of claims 1 to 11 or 14 in admixture with a physiologically acceptable diluent or carrier.

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19. A method of selectively expressing a nucleotide sequence of interest (NOI) in a target cell population which comprises introducing into said cell population an alternatively spliced molecule which incorporate said NOI.

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20. A method as claimed in claim 19 wherein said alternatively spliced molecule is also introduced into cells not within the target cell-population.

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21. A method as claimed in claim 19 or claim 20 wherein splice-functional elements within the alternatively spliced molecule direct target and non-target cells to generate, though *cis*-splicing, different mature mRNA molecules.

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22. A method as claimed in any one of claims 19 to 21 wherein the NOI expression product is not fused with any exons or partial exons from within the splice-functional elements.

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23. The use of splice-functional elements to restrict translation or expression of a nucleotide sequence of interest to specific cell types and/or environments.

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